

Methylsulfonyl Metabolites of PCBs and DDE in Human Tissues

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Methylsulfonyl metabolites of chlorinated biphenyls (MeSO₂-CBs) and *p,p'*-DDE (MeSO₂-DDEs) were determined in human adipose and liver tissues obtained at autopsy of seven Swedish individuals 47–80 years of age. Twenty MeSO₂-CBs and two MeSO₂-DDEs were found in the analyzed samples. In adipose tissue, most of the 4-MeSO₂-CBs were found at higher concentrations than the corresponding 3-MeSO₂-CBs and, in all samples of adipose tissue, 4-MeSO₂-2,2',3',4',5-pentaCB (4–87) and 4-MeSO₂-2,2',3,4',5',6-hexaCB (4–149) occurred at higher concentrations than other MeSO₂-CBs. In the liver, 3-MeSO₂-2,2',3',4',5,6-hexaCB (3–132) was by far the most abundant MeSO₂-CB, contributing to 61–82% of the sum of MeSO₂-CBs. In this tissue, most of the other 3-MeSO₂-CBs were also found at higher concentrations than the corresponding 4-MeSO₂-CBs. The ratios of the sum of MeSO₂-CBs to the sum of determined chlorinated biphenyls (CBs) were 1/250 and 1/28 in adipose tissue and the liver, respectively, calculated from the median values. The concentration of 2-MeSO₂-DDE was lower than that of 3-MeSO₂-DDE in both adipose tissue and liver, except in the liver from one of the individuals. The concentration ratios of 2-MeSO₂-DDE to 3-MeSO₂-DDE were about 10 times higher in liver than in adipose tissue. The ratios of the sum of MeSO₂-DDEs to *p,p'*-DDE were 1/455 and 1/61 in adipose tissue and liver, respectively, calculated from the median values. MeSO₂-CBs and MeSO₂-DDEs were also determined in lung tissue from one of the individuals. In this sample, the profiles of MeSO₂-CBs and MeSO₂-DDEs were similar to the profiles of these compounds in adipose tissue. **Key words:** adipose tissue, DDE, environmental pollutants, liver, methyl sulfone DDE, methyl sulfone PCB, PCBs, polychlorinated biphenyls. *Environ Health Perspect* 105:644–649 (1997)

Polychlorinated biphenyls (PCBs) and 1,1-bis(4-chlorophenyl)-2,2-dichloroethene (*p,p'*-DDE), a metabolite of the pesticide DDT, are well-known pollutants that have been found in many environmental matrices and in humans (1). The industrial use of PCBs has ceased in most countries, but objects containing these compounds are still employed and pollution may continue for a long time, e.g., from electronic equipment and building materials. DDT was a commonly used insecticide in the 1940s–1960s. In Sweden and many other industrialized countries, the usage of DDT was banned in the early 1970s and, consequently, the levels have decreased in these areas. However, DDT is still used in large quantities in countries where malaria is a serious problem (2,3). Due to the persistency of DDT compounds and the long-distance atmospheric transportation, the residue levels of the pesticide in the Western countries will probably be long-lasting.

In the metabolism of chlorinated biphenyls (CBs) and *p,p'*-DDE, corresponding methylsulfonyl (MeSO₂) metabolites can be formed via the mercapturic acid pathway (MAP) (4,5). The CBs with nonchlorinated, adjacent 3 and 4 positions and chlorine atoms in the 2, 5 or 2, 3, 6 positions of the same ring have been shown to form metabolites with the MeSO₂-group in position 3 or 4 (6). The MeSO₂-group location in MeSO₂-DDEs is limited to

either the 2 or the 3 position. The formation of methylsulfonyl metabolites of, e.g., CBs with vicinal hydrogen atoms, is initiated by cytochrome P450-mediated oxidation to arene oxide intermediates. Arene oxides with chlorine atoms on both sides of the 3,4-positions readily react with glutathione in position 3 or 4. The glutathione conjugates are transformed via MAP to cystein conjugates, which are cleaved by C-S lyase to thiol-substituted CBs (4,5). These are methylated by adenosyl-methionine to methyl sulfides, which then are oxidized to methyl sulfones via an intermediate formation of methylsulfinyl-CBs (4,5). Methylsulfonyl metabolites of CBs and *p,p'*-DDE are persistent and, due to their lipophilic character, they accumulate in adipose tissue (6–8). They may also have specific protein-binding properties that cause them to be retained in the body, e.g., 3-MeSO₂-DDE in adrenal tissue (9,10) and certain MeSO₂-CBs in lung, kidney, and uterine fluid (11–13), as demonstrated in experimental animals.

In environmental samples, MeSO₂-CBs and MeSO₂-DDEs were first identified in seal blubber from the Baltic (14); since then, such metabolites have been found in several species of animals (6) and in humans (7,8,15). Recently, MeSO₂-CBs and MeSO₂-DDEs were determined in Swedish mother's milk (16) and MeSO₂-CBs were determined in human blood plasma (17).

The toxicological significance of MeSO₂-CBs has not yet been clarified, but recently certain 3-MeSO₂-CBs were reported to be potent inducers of hepatic enzymes that are related to toxic effects (18,19). 3-MeSO₂-DDE is a potent toxicant for the adrenal cortex, e.g., in mice (9) and probably also in humans, as suggested by *in vitro* studies, showing that 3-MeSO₂-DDE is bioactivated to a tissue-binding metabolite by the human adrenal gland (10).

The occurrence of MeSO₂-CBs and MeSO₂-DDEs in wildlife and human samples and the demonstrated accumulation of certain MeSO₂-CBs and MeSO₂-DDEs in specific tissues of mammals have made the investigation of these compounds important. The knowledge of accumulation and distribution of methylsulfonyl metabolites of aromatic organochlorine pollutants in humans is scarce. Therefore, in the present study we have determined MeSO₂-CBs and MeSO₂-DDEs together with CBs and *p,p'*-DDE in adipose tissue and liver from human subjects.

Materials and Methods

Sample description. Samples of adipose tissue from the abdominal region and of liver were collected at autopsy of five men and two women (Swedish) who had suffered sudden death. The age of the men ranged from 53 to 80 years (mean 68 years, median 68 years) and the age of the women were 47 and 62 years. The samples were frozen immediately after collection, kept at -20°C, and thawed only before analysis.

Chemicals. 3-Methylsulfonyl-4-methyl-2',3',4',5,5'-pentachlorobiphenyl (MeSO₂-IS) was used as an internal standard. Individual MeSO₂-CBs, 3-MeSO₂-DDE, and MeSO₂-IS were gifts from Åke Bergman and were synthesized as described elsewhere (20–22). Structures and abbreviations of MeSO₂-CBs are given in Table 1. [4-¹⁴C]cholesterol (¹⁴C-cholesterol) and 1,2-di[1-¹⁴C]palmitoyl-*sn*-3-phosphatidyl-

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choline (^{14}C -phosphatidyl-choline) were purchased from Amersham International (Buckinghamshire, UK) and were dissolved in toluene. Organic solvents were of high purity and redistilled prior to use (24). Water was deionized and purified with a Milli-Q cartridge system (Millipore, Bedford, MA). Formic acid (98–100%) (Riedel de Haën, Seelze, Germany) was extracted twice with hexane (50 ml hexane to 100 ml formic acid). Glassware was washed thoroughly, heated overnight at 280°C, and rinsed with hexane prior to use (24).

Extraction, lipid determination, and preliminary purification. Liver (~3 g) or adipose tissue (~0.5 g) was weighed into a 100-ml test tube with a polytetrafluoroethylene (PTFE)-lined screw cap. Internal standard (50 μl of 41.4 pg MeSO_2 -IS/ μl hexane) was added and the sample was homogenized with an Ultra Turrax homogenizer (Janke & Kunkel, Germany) and extracted with hexane/2-propanol (20

ml, 3/2 v/v). The homogenate was centrifuged at 3500 rpm for 10 min and the organic solvent phase was collected in a round-bottomed flask. The extraction procedure was repeated once with hexane/2-propanol (20 ml, 3/2 v/v) and once with hexane (20 ml). The pooled organic phases were evaporated under reduced pressure at 35°C. The residue was dried in a desiccator with silica gel at room temperature and then weighed. The residue was dissolved in hexane and transferred to a 100-ml Erlenmeyer flask (samples containing more than 0.3 g lipids were diluted with hexane and an aliquot of the sample was taken to the Erlenmeyer flask). The volume of the sample solution was adjusted to 3 ml with hexane. 2-Propanol (8 ml) and formic acid (0.5 ml) were mixed with the sample solution, and 6 g Lipidex 5000 (Packard Instruments, Downers Grove, IL) (25) was added. Lipids and lipophilic compounds in the sample were transferred into Lipidex by

a liquid-gel partitioning technique described previously (25). The gel with incorporated lipophilic compounds was poured into a glass column with an inner diameter (ID) of 2 cm (26) and the solvent was drained. The gel was washed with 40 ml each of methanol-water 30:70 (v/v) and 50:50 (v/v). The chlorinated compounds and some lipids were eluted with acetonitrile (80 ml for liver samples and 110 ml for adipose tissue samples). Remaining lipids were eluted with methanol/trichloromethane/hexane (60 ml 1:1:1 by volume). The two fractions containing lipids were taken to near dryness under reduced pressure and dried to constant weight in a desiccator with silica gel. The sum of the weights of the residues in the two fractions defined the amount of lipids in the sample.

Further purification and separations.

MeSO_2 -CBs and MeSO_2 -DDEs were separated from other organochlorine compounds by adsorption chromatography using 5% water-deactivated aluminium oxide (5 g, 1 cm ID) (16). The fraction containing PCBs and p,p' -DDE was applied to activated silica gel (0.6 g, 0.5 cm ID) (26) and subsequent determinations of p,p' -DDE and CBs were made by gas chromatography (GC) electron-capture detection (Westrand and Norén, unpublished data). The fraction from the aluminium oxide column, containing MeSO_2 -CBs and MeSO_2 -DDEs, was subjected to gel permeation chromatography (GPC) on Bio-Beads S-X3 (9 g, 1 cm ID; Bio-Rad Laboratories, Richmond, CA) (17). After concentration to approximately 50 μl , the fraction was injected into a 250 μl loop. Hexane-dichloromethane (1:1 v/v) was used as the mobile phase at a flow rate of 1.0 ml/min. MeSO_2 -CBs and MeSO_2 -DDEs were collected between 22 min and 34 min. This fraction was concentrated to approximately 50 μl and injected for a second separation on the GPC system using the same procedure. The fraction containing MeSO_2 -CBs and MeSO_2 -DDEs was concentrated, an injection standard (2,2',3,3',4,4',5-heptaCB) was added, and about half of the sample was analyzed by gas chromatography-mass spectrometry (GC-MS) at a resolution of 5,000 (10% valley definition), using electron ionization and selected ion recording [for further details see Norén et al. (16)]. For each compound, two ions in the molecular ion cluster were monitored.

Preliminary study of transfer into Lipidex. Samples of human liver (~3 g) or adipose tissue (~0.5 g) were fortified with ^{14}C -cholesterol (2 μg , 33 nCi) or ^{14}C -phosphatidylcholine (0.2 μg , 25 nCi). The samples were extracted as described using 5

Table 1. Concentrations (ng/g lipids) of MeSO_2 -CBs and MeSO_2 -DDEs in adipose and liver tissue from human subjects ($n=7$)

MeSO_2 -CB	Cl substitution	Adipose		Liver	
		Median	Range	Median	Range
3-49 ^a	2,2',4',5'	0.02	0.01–0.09	0.05	0.02–0.15
4-49	2,2',4',5'	0.13	0.06–0.47	0.11	0.07–0.26
3-52	2,2',5',5'	<0.01	<0.01	<0.01	<0.01
4-52	2,2',5',5'	<0.01	<0.01	<0.01	<0.01
3-64	2,4',5',6'	0.03	0.02–0.12	0.05	0.03–0.10
4-64	2,3,4',6'	<0.01	<0.01–0.03	<0.01	<0.01–0.02
3-70	2,3',4',5'	0.04	0.02–0.12	0.05	0.03–0.16
4-70	2,3',4',5'	<0.01	<0.01	0.04	<0.01–0.07
3-87	2,2',3',4',5'	0.07	0.04–0.35	0.83	0.19–9.73
4-87	2,2',3',4',5'	0.82	0.48–3.59	1.22	0.61–2.61
3-91	2,2',4',5',6'	<0.01	<0.01	1.06	0.14–8.77
4-91	2,2',3,4',6'	0.01	<0.01–0.10	<0.01	<0.01–0.02
3-101	2,2',4',5',5'	0.17	0.07–0.85	0.29	0.04–1.63
4-101	2,2',4',5',5'	0.40	0.21–2.61	0.54	0.18–1.53
3-110	2,3',4',5',6'	<0.01	<0.01	<0.01	<0.01–0.55
4-110	2,3',4',5',6'	<0.01	<0.01	<0.01	<0.01
3-132	2,2',3',4',5',6'	0.07	<0.02–0.29	19.8	8.37–276
4-132	2,2',3,3',4',6'	0.04	<0.02–0.29	0.07	<0.02–0.25
3-141	2,2',3',4',5',5'	0.03	<0.02–0.19	0.06	<0.02–0.25
4-141	2,2',3',4',5',5'	0.19	0.12–0.91	0.23	0.11–0.36
3-149	2,2',4',5',5',6'	0.33	0.17–2.81	2.01	0.58–38.0
4-149	2,2',3,4',5',6'	0.71	0.41–5.06	1.69	0.69–11.2
3-174	2,2',3',4',5',5',6'	<0.03	<0.03–0.13	0.21	0.07–6.49
4-174	2,2',3,3',4',5',6'	<0.03	<0.03–0.05	<0.03	<0.03
Sum of MeSO_2 -CBs		2.93	2.02–8.96	28.4	11.8–358
2- MeSO_2 -DDE		0.07	<0.02–0.38	4.58	0.38–15.9
3- MeSO_2 -DDE		1.39	0.12–8.88	13.3	0.41–31.1
Sum of MeSO_2 -DDEs		1.47	0.12–9.26	17.9	0.88–47.1
2- MeSO_2 -DDE/ 3- MeSO_2 -DDE		0.04	0–0.09	0.36	0.32–1.15
p,p' -DDE		707	121–1394	925	155–1662
Sum of CBs		977	492–1993	801	415–2052
CB-153		275	136–586	233	111–612
Sum of MeSO_2 -DDEs/ p,p' -DDE		0.002	0.001–0.007	0.016	0.005–0.033
Sum of MeSO_2 -CBs/ CBs		0.004	0.002–0.012	0.036	0.015–0.175
Sum of MeSO_2 -CBs/ CB-153		0.012	0.008–0.042	0.128	0.053–0.586

^aPCB congener number of parent compound according to Ballschmiter et al. (23).

or 6 g Lipidex 5000 and with different mixtures of hexane, 2-propanol, and formic acid. The gel with sorbed lipophilic compounds was eluted with acetonitrile as described above. The volumes of the fractions from the Lipidex column were measured and 0.5 ml aliquots were taken for determination of radioactivity (24).

Results

In the preliminary study of transfer of lipophilic compounds into Lipidex, the recoveries of ^{14}C -cholesterol and ^{14}C -phosphatidylcholine added to samples of adipose tissue and liver from human subjects prior to homogenization were 92–105% and 97–98%, respectively.

The concentration of lipids in adipose tissue and liver from the seven subjects ranged from 52 to 99% and from 3 to 23%, respectively. The recoveries of the internal standard, $\text{MeSO}_2\text{-IS}$, added to all samples prior to homogenization ranged from 67 to 103% (mean 83%; $n = 14$). The recoveries of $\text{MeSO}_2\text{-IS}$ have been shown to correlate well with the recoveries of $\text{MeSO}_2\text{-CBs}$ (16,17) and 3- $\text{MeSO}_2\text{-DDE}$ (16).

The concentrations of $\text{MeSO}_2\text{-CBs}$ and $\text{MeSO}_2\text{-DDEs}$ varied in the different subjects (Table 1); therefore, mean values were not calculated for the individual compounds. However, the profiles of $\text{MeSO}_2\text{-CBs}$ and $\text{MeSO}_2\text{-DDEs}$ (Figs. 1, 2, and 3) were similar in all seven subjects.

In adipose tissue and liver, most of the penta- and hexachloro-substituted congeners were found at higher concentrations than the other $\text{MeSO}_2\text{-CBs}$ (Table 1, Fig. 1). In adipose tissue, the pentaCB methyl sulfone 4-87 and the hexachloro compound 4-149 were found at highest concentrations (Fig. 2). In the liver, compound 3-132 was found at a higher concentration than any of the other aryl methyl sulfones; the contribution of this compound to the sum of $\text{MeSO}_2\text{-CBs}$ ranged from 61% to 82% in the individual samples. In adipose tissue, the concentration of 3-132 was low, only 0–4% of the sum of $\text{MeSO}_2\text{-CBs}$. In the liver, the sum of 3- $\text{MeSO}_2\text{-CBs}$ was higher than the sum of 4- $\text{MeSO}_2\text{-CBs}$. The ratios of the sums of 3- $\text{MeSO}_2\text{-CBs}$ to 4- $\text{MeSO}_2\text{-CBs}$ ranged from 4 to 21 in the liver samples. Only compounds 4-49, 4-87, 4-101, and 4-141 were found at higher concentrations than the corresponding 3- $\text{MeSO}_2\text{-substituted}$ congeners. In adipose tissue, the ratios of the sums of 3- $\text{MeSO}_2\text{-CB}$ to 4- $\text{MeSO}_2\text{-CBs}$ were below 1 (0.2–0.5) in all subjects, and only compounds 3-64, 3-70, and 3-174 were found in larger amounts than the corresponding 4- $\text{MeSO}_2\text{-CBs}$.

The sum of the determined CBs was similar in adipose tissue and liver in paired

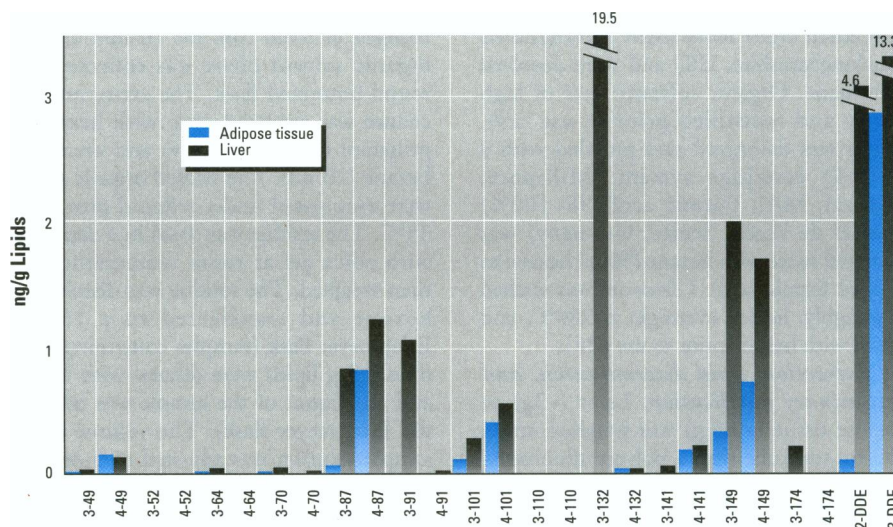


Figure 1. Concentrations of $\text{MeSO}_2\text{-CBs}$ (for structures see Table 1), 2- $\text{MeSO}_2\text{-DDE}$ (2-DDE), and 3- $\text{MeSO}_2\text{-DDE}$ (3-DDE) in human adipose tissue and liver (74 year-old man).

samples (Weistrand and Norén, unpublished data). In contrast, the sum of the concentrations of $\text{MeSO}_2\text{-CBs}$ was significantly higher in the liver than in adipose tissue in all cases. The ratios of the sum $\text{MeSO}_2\text{-CBs}$ to the sum of CBs were 8–34 times higher in the liver than in adipose tissue as calculated from the individual values.

Two methyl sulfone metabolites of p,p' -DDE were found in the samples (Figs. 1, 3, Table 1). We lacked authentic 2- $\text{MeSO}_2\text{-DDE}$, but comparison with studies where this compound has been identified (6) suggests that the peak appearing ahead of 3- $\text{MeSO}_2\text{-DDE}$ in the selected ion current chromatogram represents 2- $\text{MeSO}_2\text{-DDE}$ (Fig. 3). Assuming that 2- $\text{MeSO}_2\text{-DDE}$ has the same response as 3- $\text{MeSO}_2\text{-DDE}$, the concentrations of 2- $\text{MeSO}_2\text{-DDE}$ were lower than those of 3- $\text{MeSO}_2\text{-DDE}$ in all samples, except in the liver sample from one of the female subjects (47 years old). The ratios of 2- $\text{MeSO}_2\text{-DDE}$ to 3- $\text{MeSO}_2\text{-DDEs}$ were about 10 times higher in liver than in adipose tissue (Table 1).

The concentrations of p,p' -DDE were similar in liver and adipose tissue in the individual subjects. The concentrations of the methyl sulfone metabolites of p,p' -DDE were higher in liver than in adipose tissue in all individuals. The ratios of the sum of $\text{MeSO}_2\text{-DDEs}$ to p,p' -DDE were 2–28 times higher in the liver than in adipose tissue as calculated from individual values.

In addition, a sample of lung tissue (2 g) was collected from one of the male subjects (68 years old) and was treated and analyzed using the same procedure as described for the liver samples. The ratios of the sum of $\text{MeSO}_2\text{-CBs}$ and $\text{MeSO}_2\text{-DDEs}$ to the sum of CBs and p,p' -DDE, respectively,

were very similar in lung and adipose tissue from this individual. Also, the profile of $\text{MeSO}_2\text{-CBs}$ and $\text{MeSO}_2\text{-DDEs}$ in lung resembled the profile of these compounds in adipose tissue. However, 2- $\text{MeSO}_2\text{-DDE}$ was not detected in the lung.

Discussion

In a previous study using Lipidex for extraction of PCBs and lipids in fish oil (25), the lipids mainly consisted of triacylglycerols. To validate the method for cholesterol and more polar phospholipids occurring in the liver, recovery studies were performed with ^{14}C -cholesterol and ^{14}C -phosphatidylcholine added to liver and adipose tissue from human subjects. Slight modifications of the previous method were made to achieve satisfactory recoveries. The ratio of hexane to 2-propanol was changed, formic acid added, and the amount of Lipidex increased.

In the present study, most of the investigated $\text{MeSO}_2\text{-CBs}$ (Table 1) were found in human adipose tissue and liver. However, most of the parent compounds to these $\text{MeSO}_2\text{-CBs}$ were below the detection limits in the tissues. Only low levels were found of 2,2',5,5'-tetraCB (CB-52), 2,2',4,5,5'-pentaCB (CB-101), and 2,2',3,3',4,5,6'-heptaCB (CB-174).

In adipose tissue, most of the 4- $\text{MeSO}_2\text{-CBs}$ were present at higher concentrations than the corresponding 3- $\text{MeSO}_2\text{-CBs}$; congeners 4-87 and 4-149 were found at the highest concentrations. These were also the major congeners in Swedish human milk (16) and blood plasma (17). In addition, the concentration ratios of $\text{MeSO}_2\text{-CBs}$ to CB-153, which is a stable and predominant CB in mammals, were similar in

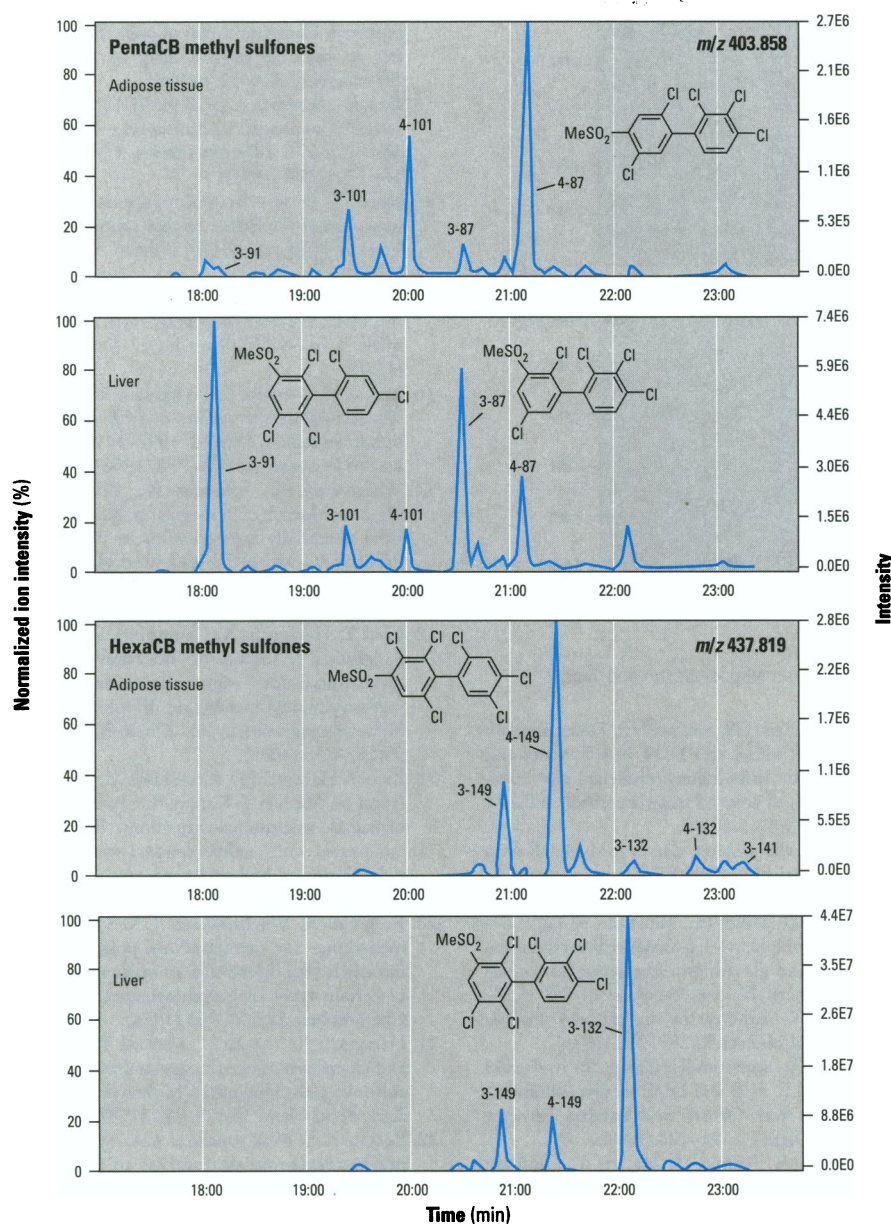


Figure 2. Selected ion current chromatograms of MeSO₂-CBs in human adipose tissue and liver.

the adipose tissue samples (0.008–0.042), Swedish human milk (0.02–0.04) (16), and blood plasma (0.002–0.03) (17).

The profiles of MeSO₂-CBs in the Swedish samples (human milk, blood plasma, adipose tissue, lung, liver) differed from those in a Japanese investigation (7). In the latter, compound 4-87 was the most abundant MeSO₂-CB in adipose and lung tissue from a Yusho patient, but not in the samples from a control subject. 4-MeSO₂-2,4',5-triCB was the most abundant MeSO₂-CB in adipose tissue from the control subject, while 4-MeSO₂-2,3',5-triCB was found at highest concentration in the liver from this individual (7). In contrast, MeSO₂-CBs with two or three chlorine atoms were not found in the

GC-MS analyses of adipose tissue and liver from the Swedish subjects. Compound 3-132 was by far the predominant MeSO₂-CB in the liver samples from Swedish subjects; also, most of the other identified 3-MeSO₂-CBs were found at higher concentrations than the corresponding 4-MeSO₂-CBs in this tissue. The differences between the Japanese and Swedish profiles of MeSO₂-CBs may be due to different sources of exposure and/or metabolism of CBs.

The profiles of MeSO₂-CBs in wild animals differ from those in humans and have also been found to vary in different animal species (6). In muscle or blubber from Swedish wildlife (otter, mink, grey seal), 3-101 was the predominant MeSO₂-CB, but

the corresponding 4-MeSO₂-CB was also found at high concentrations (6). A similar profile has been found in polar bear fat from Canada, but 3-87 and 4-87 were also found at high concentrations (6,27). In livers from Swedish wild animals (grey seal, otter, mink) and Canadian polar bears, 3-149 and 3-87 were the most abundant MeSO₂-CBs, respectively (6,28). The different pattern of MeSO₂-CBs indicate differences in exposure and/or metabolism of CBs.

Toxicological studies of MeSO₂-CBs have indicated that compounds 3-49, 3-87, and 3-101 were, of the tested MeSO₂-CBs, the most potent inducers of certain hepatic enzymes (29). Compound 3-132, which was found at high concentrations in the present investigation of human liver, was shown to be a weak inducer of these enzymes (29).

The retention of certain 3-MeSO₂-CBs in livers of wild mammals (6,28) and in humans indicates that MeSO₂-CBs with such structures are noncovalently bound in the liver, probably to proteins. Such binding has been described between certain 4-MeSO₂-CBs and a uteroglobin-type protein (12) and a fatty acid binding protein (FABP) (30–32). In addition, it has been shown that a 3-MeSO₂-CB (3-101) binds to FABP (rat liver) (32).

Two MeSO₂-DDEs were identified in the adipose tissue and liver samples from the Swedish subjects. Both in adipose tissue and liver, 3-MeSO₂-DDE was found at higher concentrations than 2-MeSO₂-DDE. In adipose tissue, 3-MeSO₂-DDE was the predominant aryl methyl sulfone and 2-MeSO₂-DDE was only found at low concentrations, about 1/20 of the concentration of 3-MeSO₂-DDE. Low levels of 2-MeSO₂-DDE were also found in Swedish human milk (16) and in Japanese adipose tissue and liver (7). In the Swedish liver samples, 3-MeSO₂-DDE was one of the most abundant aryl methyl sulfones, but it was found at lower concentrations than 3-MeSO₂-2,2',3',4',5,6-hexaCB (3-132). 2-MeSO₂-DDE was the third most abundant aryl methyl sulfone and was found at about one-third of the concentration of 3-MeSO₂-DDE. The sum of the concentrations of MeSO₂-DDEs and the ratio of 2-MeSO₂-DDE to 3-MeSO₂-DDE were higher in the liver than in adipose tissue, which indicates selective binding in the liver. In wild mammals, the ratio of 2-MeSO₂-DDE to 3-MeSO₂-DDE in these tissues, has been found to vary with species and tissue, and the results indicate differences in exposure and/or metabolism of DDT/DDE (6).

Conclusions

In the present study, MeSO₂-CBs and MeSO₂-DDEs were determined together

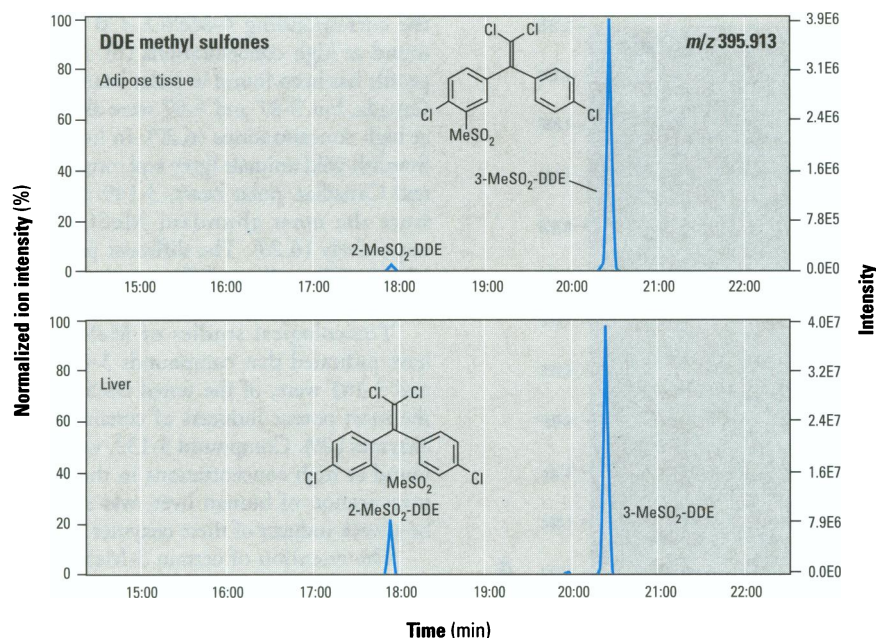


Figure 3. Selected ion current chromatograms of MeSO₂-DDEs in human adipose tissue and liver.

with CBs and *p,p'*-DDE in tissues from seven Swedish human subjects. MeSO₂-CBs and MeSO₂-DDEs were found in all samples showing a general occurrence of these metabolites together with CBs and *p,p'*-DDE. The profiles of MeSO₂-CBs and MeSO₂-DDEs were similar in adipose tissue and lung. A different pattern was found in the liver. The concentrations of CBs were similar in adipose tissue and the liver. This was also the case for *p,p'*-DDE. However, the methyl sulfonyl metabolites of these compounds were significantly higher in liver than in adipose tissue (lipid weight basis). In the human liver, 3-MeSO₂-2,2',3',4',5,6-hexaCB (3-132) was by far the predominant MeSO₂-CB. Certain 3-MeSO₂-CBs have previously been found to be selectively retained in the livers of different wild mammals. This indicates that certain structures of MeSO₂-CBs facilitate noncovalent binding in the liver, most probably to proteins. Also, the metabolites may have toxic effects. However, little is known about the toxicity and possible effects in humans; therefore this subject requires further study.

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VI International Symposium of the International Section of the ISSA for the Prevention of Occupational Risks in the Iron and Metal Industry



Safety Health at the Workplace Competitiveness

Barcelona, Spain October 20-22, 1997

The main themes of the symposium are:

- Management, organization, and control in the field of safety and health in the workplace (programs, risk analysis, assessment, normalization, quality...)
- Specific problems of occupational safety and health in small- and medium-sized enterprises as well as possibilities for counseling and support
- Current problems of occupational hygiene (dust, mineral fibers, surface treatments)

Furthermore, the symposium will discuss other current problems and solutions, such as the transposition of European Directives or outsourcing.

Target groups

The symposium is aimed at safety engineers, occupational physicians, and hygienists, human resources managers, management representatives, experts in various fields from the industry, representatives of the social partners, social insurance institutions, and the authorities.

The symposium is organized by the International Section of the International Social Security Association (ISSA) for the Prevention of Occupational Risks in the Iron and Metal Industry, whose Secretariat is represented by the Allgemeine Unfallversicherungsanstalt (AUVA) in Vienna, together with the Asociación para la Prevención de Accidentes (APA) in Spain.

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